SBAR: Immune Globulin for Post-exposure Prophylaxis

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Situation

Immune globulin (IG) is recommended for the postexposure prophylaxis (PEP) of contacts to hepatitis A virus (HAV) and measles. The Bureau of Communicable Disease Control and Prevention (BCDCP) has historically purchased and maintained IG to ensure it was promptly available for contacts to HAV and measles cases. However, there is no line item in BCDCP's budget or specific appropriation for purchasing IG, so state general revenue has been used to pay for the cost of IG, if funds were available at the end of each fiscal year. The Centers for Disease Control and Prevention (CDC) recently released new recommendations for HAV PEP increasing the dose of IG by fivefold[1]. With the increase in dosing for HAV and the large dose already required for measles, BCDCP will no longer be able to routinely purchase IG for this purpose. BCDCP is seeking to coordinate with local public health agencies and other key stakeholders to identify alternative options to assure prompt availability and access to IG for HAV and measles contacts in Missouri.

Background

Hepatitis A virus infection is acquired primarily by the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water. Infected persons are most likely to transmit HAV 1 to 2 weeks before onset of symptoms to 1 week after the onset of jaundice. Immune globulin is recommended for the PEP of contacts to HAV that have not been previously vaccinated or do not have evidence of immunity. To be effective, the IG must be given within 14 days of exposure to HAV. On September 15, 2017, the CDC released new recommendations for HAV PEP that increases the dosage of IG from .02 mL/kg to .10 mL/kg with no upper limit for each contact[1]. Immune globulin is recommended for contacts less than 12 months of age; 41 years of age or older; and persons of any age who are immunocompromised, have chronic liver disease, or contraindication to vaccination. A dose of HAV vaccine is recommended for PEP for persons 12 months through 40 years of age.

Measles is a highly contagious virus that is transmitted person-to-person among close contacts by direct contact with infectious droplets or less commonly, by airborne spread. Measles may be transmitted from 4 days before to 4 days after rash onset. Measles vaccine is recommended PEP for vaccine-eligible persons, if given within 72 hours of exposure. Immune globulin is recommended for the PEP of contacts to measles that have not been previously vaccinated or do not have evidence of immunity. The recommended dose required for each contact of measles is 0.50 mL/kg up to 15 mL[2]. If administered within 6 days of exposure, IG can prevent or modify measles in persons who are susceptible. Immunoglobulin is indicated for susceptible close contacts of persons with measles, particularly infants less than 12 months of age. Immune globulin can be administered to other persons who do not have evidence of measles immunity. Pregnant women and severely immunocompromised persons are also

[1] CDC. Updated Dosing Instructions for Immune Globulin (Human) GamaStan S/D for Hepatitis A Virus Prophylaxis. *MMWR* 2017;66:959-960. https://www.cdc.gov/mmwr/volumes/66/wr/mm6636a5.htm

[2] Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL. American Academy of Pediatrics; 2015: Hepatitis A, 394.

recommended to receive IG. However, due to the increased risk for severe measles, intravenously administered IG (IGIV) is recommended for these persons. The IGIV for this purpose is not purchased or provided by BCDCP.

Assessment

The average cost per adult for HAV PEP is now $700 and $3,500 per adult for measles. BCDCP currently has 20 mL of IG in stock, which is enough to provide PEP for 2 average weight adults exposed to HAV or 1 average adult exposed to measles. An average of 22 (range, 9 to 45) HAV cases have been reported during the years 2007-2016. A preliminary total of 25 cases have been reported in 2017. A total of 41 cases of measles were reported during the years 2007-2016. Twenty-seven of these cases were associated with a single measles outbreak that occurred in Northwest District in 2014. No measles cases have been reported in Missouri in 2017. The overall number of contacts to HAV or measles cases that received prophylaxis with IG during this time period is not known. The amount of IG needed, the shelf-life of the IG received, and overall availability of the product can vary greatly, further adding to the overall costs of maintaining IG for this purpose.

Several large outbreaks of HAV are currently ongoing in multiple states. As of January 2, 2018, California had 683 reported outbreak-associated hepatitis A cases, Kentucky had 31, Michigan had 630, and Utah had 124 cases. Common risk factors for these outbreaks are homelessness and drug use. These risk factors are troubling, since they indicate that the at-risk population may be more transient than the general population. This means that the potential for a related large-scale outbreak is possible in Missouri. Measles is no longer endemic in the U.S. though travel associated cases continue to occur. A preliminary total of 120 cases of measles have been reported in the U.S. in 2017. Measles is highly communicable and outbreaks can still occur in Missouri. Measles case and outbreak investigations are challenging and very labor intensive.

Cases of HAV and measles will continue to be reported in Missouri resulting in the identification of susceptible contacts in need of PEP. Immune globulin will need to be available for these contacts in a timely manner to protect the health of the individual contact and the overall public's health. The time required for the diagnosis, reporting, and investigation of HAV and measles cases often limits the amount of time for public health to identify and assist in providing PEP to contacts. With state level public health resources unavailable for this purpose, collaboration with hospital and healthcare systems within the state to ensure the timely availability of IG to prevent HAV and measles is essential.

Recommendations

BCDCP proposes to form a workgroup to determine the best method to communicate the need for IG availability within the healthcare system in Missouri. Some possibilities for the workgroup to discuss are:

- BCDCP can reach out directly to hospital systems or through the Missouri Hospital Association
- Local public health agencies can reach out to the hospital systems in their area
- BCDCP and local public health agencies can reach out to hospital systems in a collaborative effort